UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,240	09/19/2003	Tommy Ekstrom	06275-188002	6971

26164 7590 06/12/2009

FISH & RICHARDSON P.C.
P.O BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
CARTER, KENDRA D	
ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
06/12/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/665,240	EKSTROM, TOMMY	
	Examiner	Art Unit	
	KENDRA D. CARTER	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-29,34,36 and 42-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-29,34,36 and 42-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/367,950.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/27/09;4/6/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner acknowledges the Applicant's remarks and arguments of March 18, 2009 made to the office action filed September 19, 2008. Claims 13-29, 34, 36 and 42-56 are pending. Claims 49-51 are amended and claims 52-56 are new.

The Examiner acknowledges Applicant's indication that a terminal disclaimer will be filed upon identification of allowable subject matter to obviate the provisional obviousness-type double patenting rejections over U.S. Patent Application No. 09/367,950. However, as such terminal disclaimers have not as-yet been filed, the provisional obviousness-type double patenting rejections over these co-pending applications are being maintained. The Examiner has modified the heading to reflect the claims that are pending.

For the reasons in the previous office action and below, the Applicant's arguments of the 35 U.S.C. 103(a) rejection of claims 13-15, 17, 18, and 20-29, 34, 36 and 42-51 as being unpatentable over Carling (WO 9311773 A1) were found not persuasive, thus the rejection is upheld.

For the reasons in the previous office action and below, the Applicant's arguments of the 35 U.S.C. 103(a) rejection of claims 16 and 19 as being unpatentable over Carling as applied to claims 13-15, 17, 18, and 20-29, 34, 36 and 42-51 above in

view of Aberg et al. and in further view of Ryrfeldt et al, were found not persuasive, thus the rejection is upheld.

Due to the amendment to the claims, the modified and new 35 U.S.C. 103(a) and double patenting rejections are made below.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 13-15, 17, 19, 20, 22-25, 34, 36, 42 and 53 are provisionally rejected on the ground of nonstatutory double patenting over claims 13-15, 17, 19, 20, 22-25, 30-

36, 38, and 42 of copending Application No. 09/367,950. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

The US Application No. 09/367,950 discloses a method of prevention and treatment of asthma symptoms, which comprises instructing a patient in need thereof to inhale an effective amount of a composition comprising, in admixture: (a) a first active ingredient which is formoterol, a pharmaceutically acceptable salt or solvate thereof or a solvate of such a salt; and (b) a second active ingredient which is budesonide; characterized in that the patient is instructed to inhale the composition on demand, as determined by the patient based on the patient's symptoms, as a treatment and a preventive measure, when the patient experiences an increase in asthma symptoms (see claims 13 and 42). The molar ratio of (a) to (b), calculated as formoterol to

budesonide~ is from 1:1 to 1:100 or 1;1 to 1:70 (see claims 14 and 25). The first active ingredient can be formoterol fumarate dihydrate (see claim 15) or the R,R enantiomer of formoteml, a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt (see claim 16). Formoterol is in a unit dose of from 1 μg to 48 μg or 1 μg to 100 μg for daily dose, including maintenance therapy, which is calculated as formoterol fumarate dihydrate (see claims 13, 17 and 42). The second active ingredient can be the 22R epimer of budesonide (see claims 13, 19 and 42). The budesonide is in the form of a unit dose, which delivers 20 μg to 1600 μg to the patient (claim 20. The particle size of the active ingredients (a) and (b) is less than 10 μm (see claim 22). The composition additionally comprises one or more pharmaceutically acceptable additives, diluents or carriers (see claim 23). The composition can comprise lactose monohydrate (see claim 24). The patient can be instructed to inhale the composition as a rescue medication, as a complement to maintenance treatment of the patient's asthma, as a preventive measure prior to encountering an asthma triggering event, such as cold air, exercise, and exposure to a smoky environment (see claims 34 and 36).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject

matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(1) Claims 13-15, 17, 18, and 20-29, 34, 36 and 42-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carling (WO 9311773 A1).

Carling et al. teaches suitable daily asthmatic dose of formoterol (as fumarate dihydrate; see page 8, line 6; addresses applicant's claims 13, 15, 17-18, 26-27, 36, 42 and 49-56) and/or a physiologically acceptable salt and/or solvent thereof and budesonide twice a day (i.e. on demand; see page 4, lines 24-28; page 6, lines 5-30, addresses applicant's claims 13, 35, 36, 42 and 49-51). The combination of the two drugs have greater efficiency and duration of bronchodilator action, and rapid onset action, which provides rescue medicine, adequate dosing for treating asthma (see page 4, lines 4-21; addresses applicant's claims 13, 36, 42 and 49-51). This new feature is of utmost importance in order to establish a higher compliance for patients and it provides a rescue medicine thereby avoiding the necessity for the patient of carrying two different inhalers (see page 4, lines 4-10; addresses claim 48). Formoterol is administered in a suitable daily dose in a range of 6 to 100 μg with a daily dose of budesonide in a range of 50 to 4800 μg (see page 6, lines 24 and 26; addresses applicant's claims 17, 18, 20, 21, and 27-29). The dosages strongly depends on the patient (age, weight etc.), severity of disease (mild, moderate, severe asthma etc..); see page 6, lines 27-29. The ratio of formoterol to budesonide is in the range of 1:4 to 1:70, which can be

administered separately in the same ratio (see page 6, lines 17-20; addresses applicant's claims 14, 17, 20, 25, 26, and 28). Non-toxic and chemically inert diluents, additives, and carriers are used in the composition, such as lactose (see page 7, lines 1-3; addresses applicant's claim 23 and 24). The amounts of active agents per dose of inhalation are disclosed on pages 7-9, which calculate up to 8 inhalation per day without going over the maximum daily dosage. For administration, the combination is suitably inhaled from a nebulizer, from a pressurized metered dose inhaler or as a dry powder from a dry powder inhaler (see page 6, last paragraph, addresses claims 43 and 44). The micronized mixture may be suspended in a liquid propellant mixture. The propellants may be chlorofluorocarbons of different chemical formulae. The most frequently used chlorofluorocarbon propellants include tetrafluoroethane (P134a) and 1,1-difluoroethane (P152a; see page 7, lines 15-25; addresses claims 45-47).

Carling et al. does not specifically teach one or more additional doses on an irregular, as-needed basis for rescue purposes, as determined by the patient (claim 13), based on the patient's symptoms, when (1) the patient experiences an increase in asthma symptoms as set forth in applicant's claim 13; or (2) when the patient is expecting to encounter an asthma inducing condition, wherein the inducing condition is selected from the group consisting of exposure to cold air, exposure to pollen, exposure to perfume, exercise, or exposure to a smoky environment (applicant's claims 34, 36, 50 and 51). Carling et al. does not teach to inhale additional doses as needed to improve control and provide acute relief (applicant's claim 42). Carling et. al. also does not

teach the particle size of the active ingredients (applicant's claim 22), or the specific propellant P227 (claim 47).

To one of ordinary skill in the art, it would have been obvious to combine the method of Carling et al. and administering the method on an irregular, as-needed basis for rescue purposes, as determined by the patient in any of the circumstances detailed in claims 13, 34, 36, 42 and 49-51 because Carling et al. teaches that the dosages strongly depends on the severity of disease, whether mild, moderate, or sever asthma (see pg 6, lines 27-29), and the suitable daily dosage is up to 8 inhalation (see page 7-9).

The motivation to combine the methods and compositions of Carling et al. and instructing the patient to inhale, on demand in any of the circumstances detailed in claims 13, 34, 36, 42 and 49-51 because Carling et al. teaches that the dosages strongly depends on the severity of disease and to achieve maximum benefit of daily dosage recommended. It is noted by Carling et al. that the combination of formoterol with budesonide is well known to be beneficial for the treatment of asthma (see page 4, lines 4-21). Moreover, if the patient is experiencing acute asthmatic attack even with ongoing twice a day dosing regimen, the patient can still safely inhale an additional 6 inhalations without going over the maximum suitable daily dosage. In general, Carling et al. teaches therapeutic relief from asthmatic attack. The skilled artisan would have

been motivated to instruct the patient to use the Carling et al. composition as needed on the bases of up to 8 inhalations a day is for reasonable expectation of successfully achieving maximum benefit in the treatment of any level of the asthma condition, including an increase in asthma symptoms, acute asthmatic condition, maintenance treatment, and common asthma triggers. Additionally, due to the urgency of therapy during an asthma attack, a patient would obviously seek relief with the medication without consulting with the physician, in knowing the safe daily dosage range of each medication.

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine the method of Carling et al. and the particle size of active agents set forth in claim 22, because they are known by a skilled pharmacologist and represent conventional formulations.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Carling et al. and the specific propellant P227 because Carling et al. teach that the propellants may be chlorofluorocarbons of different chemical formulae. Carling et al. also teaches some of the most frequently used, such as Applicant's claimed tetrafluoroethane (P134a) and 1,1-difluoroethane (P152a; see page 7, lines 15-25; addresses claims 45-47).

(2) Claim 16 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carling et al. of record as applied to claims 13-15, 17, 18, and 20-29, 34, 36 and 42-56 above, in view of Aberg et al. (U.S. Patent 5,795,564) and in further view of Ryrfeldt et al. (Biochemical Pharmocology, 1989, 38(1), pages 17-22).

Carling et al. teaching are as applied to claims 13-15, 17, 18, and 20-29, 34, 36 and 42-56 above.

Carling et al. does teach the (R,R) enantiomer of formoterol set forth in claim 16 and the 22R epimer of budesonide set forth in claim 19.

Aberg et al. teaches (R, R) isomer of formoterol as required by claim 16 is a potent bronchodilator with reduced adverse effects in treatment of asthma. (abstract, column, 1, lines 25-35).

Ryrfeldt et al. teaches that the 22R epimer of budesonide is more potent in the treatment of bronchial asthma than 22S epimer (see page 17, column 1, paragraph 2, lines 12-15).

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine the method of Carling et al. and the (R,R) enantiomer of formoterol

and the 22R epimer of budesonide because Aberg et al. and Ryrfeldt et al. teach that these specific isomers possess potent asthmatic effect.

The motivation employ the (R,R) isomer of formoterol and 22R epimer of budesonide in the Carling et al. composition is because there is a reasonable expectation of successfully treating asthmatic patients with a more effective medication with reduced adverse effects.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

> The Applicant argues that the total daily dose taught by Carling is inextricably linked to the twice daily administration regime. There is no teaching in Carling that the patient should decide for himself when to increase or decrease the daily dosage. Regardless of the number of doses inhaled at each of the two daily administrations (i.e. morning or evening), the number of daily administrations does not change. Thus, although explicitly acknowledging the fact that Carling teaches "twice a day" administration, the Office action then inexplicably seems to equate "twice a day with "on demand (see page 6 of last office action, last 7 lines). Carling et al. does not teach to inhale additional doses as need to improve control and provide acute relief. The factors in regards to age, weight, etc is for the physician to consider and not the patient. Further, regardless of the number of doses inhaled at each of the two daily administrations, the number of daily administrations does not change. Carling does not say that the patient should use the combination when experiencing an acute asthmatic attack.

The Examiner continues to disagree for the same reasons given before and repeated below. One of ordinary skill in the art would be motivated and found it obvious to combine the method of Carling et al. and administering the method on an irregular, as-needed basis for rescue purposes, as determined by the patient in any of the circumstances detailed in claims 13, 34, 36 and 42 because Carling et al. teaches that the dosages strongly depends on the severity of disease, whether mild, moderate, or sever asthma (see pg 6, lines 27-29), and the suitable daily dosage is up to 8 inhalation (see page 7-9). The motivation to combine the methods and compositions of Carling et

al. and instructing the patient to inhale, on demand in any of the circumstances detailed in claims 13, 34, 36 and 42 because Carling et al. teaches that the dosages strongly depends on the severity of disease and to achieve maximum benefit of daily dosage recommended. It is noted by Carling et al. that the combination of formoterol with budesonide is well known to be beneficial for the treatment of asthma (see page 4, lines 4-21). Moreover, if the patient is experiencing acute asthmatic attack even with ongoing twice a day dosing regimen, the patient can still safely inhale an additional 6 inhalations without going over the maximum suitable daily dosage. In general, Carling et al. teaches therapeutic relief from asthmatic attack. The skilled artisan would have been motivated to instruct the patient to use the Carling et al. composition as needed on the bases of up to 8 inhalations a day is for reasonable expectation of successfully achieving maximum benefit in the treatment of any level of the asthma condition, including an increase in asthma symptoms, acute asthmatic condition, maintenance treatment, and common asthma triggers. Additionally, due to the urgency of therapy during an asthma attack, a patient would obviously seek relief with the medication without consulting with the physician, in knowing the safe daily dosage range of each medication.

> The Applicant further argues that the Examiner's arguments of Exhibit 1 and 3-5 are not clear and provides a teaching-away from the present invention and not unexpected results. The Examiner appears to believe that, because Exhibit 1 concerns a product that contains only budesonide as an active ingredient, it cannot be used to support a teaching-away from the presently claimed methods. The Examiner has not explained why statements in Exhibit 2 does not convince her that it was never left to the patient to decide to vary the dosage. Lastly, the Examiner inexplicable

> dismisses Exhibit 3 solely because it concerns two drugs not even claimed in the current application. In Exhibits 4 and 5, a misunderstanding of what is disclosed is apparent, in that the only admixture used in the trials in Exhibit 4 contain budesonide and formoterol. The patients on this regimen do not use terbutaline as a reliever. Exhibit 5 shows that 7 years after Calring, the Applicant's invention is remarkable, is a surprisingly good result, and may lead to changes in the paradigm of asthma management.

The Examiner maintains the previous arguments and repeats that the evidence provided in Exhibit 1 is not commensurate to scope with the claimed invention because the Exhibit 1 is administration of budesonide as the sole active ingredient, while the claimed invention is an admixture of budesonide and formoterol. In regards to Exhibit 2, the statements D and E verifies the Examiner's statement that patients will take more than the current dose if needed. Although the additional doses are not recommended, it is not impossible to not take an additional administration if the patient feels the need for treatment. In an asthma attack, if a patient is faced with not breathing and taking an additional administration within the safe inhalation amounts, one would find that the patient would take an as-needed administration. Further, if the patient did not need the additional administration, the prior art clearly reads on the claimed invention. In regards to Exhibit 3, the admixture is of fluticasone and sameterol xinafoage, which are two drugs not even claimed in the current application. In regards to Exhibits 4 and 5, the Examiner agrees that budesonide and formoterol were both used for maintenance and relief (i.e. demand), but does not find that the evidence overcomes the prior art for the reasons stated above. Carling et al. teaches that the combination of budesonide and formoterol have greater efficiency and duration of bronchodilator action, and rapid onset action, which provides rescue medicine, adequate dosing for treating asthma (see page

4, lines 4-21), thus the Applicant's results are not viewed as surprising. The combination of Carling et al. provides suitable daily doses for asthma, but does not completely eliminate a patient taking more than two administrations a day. Suitable daily treatment is dependent on the patient's severity of the condition, weight, height, and age. Again, just because the combination is recommended to be taken twice daily does not mean that changes could not be made to accommodate the patient. Thus, the prior art reads on the patient taking an additional as-needed administration of the combination treatment.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/K. D. C./
Examiner, Art Unit 1617

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617